IX. "Contributions to the Physiology of the Liver.—The Influence of an Acid in producing Saccharine Urine." By F. W. Pavy, M.D. Communicated by Dr. Sharpey. Received June 13, 1861.

In 1854 I conducted an experiment to determine the effect of depriving the blood of its natural alkalinity. I then wished to see if I could influence the presumed destruction of sugar in the blood during its transit through the lungs. Phosphoric acid (Pharmacopœia strength), to the extent of $7\frac{1}{2}$ fluid drachms, was injected into the jugular vein of a dog, and the blood of the arterial system became strongly charged with sugar. Since this experiment was performed, it has been ascertained that there is not the difference during life in the blood on the two sides of the lungs that was formerly supposed to exist; and it has become evident that it was not to arresting any change in the lungs, as I at first supposed, that the result I obtained was due. The fact of the blood being rendered saccharine, led me to infer that a saccharine state of the urine might also be occasioned; and in order to settle this point I undertook the experiments that form the subject of my present communication.

In seven instances I have tried the effect of injecting phosphoric acid into the general circulation. I find that it is an experiment which requires to be performed with the greatest nicety: the animal withstands the introduction of the acid to a certain extent without manifesting any disturbance, and it may even, at first, be injected pretty rapidly; but when a certain amount, varying in different instances according to the size of the animal, has been introduced, the further introduction requires to be made most slowly and with the utmost care, attentively watching its effects; otherwise destruction of life will be occasioned. I have found this to occur in one case after one ounce had been employed, and in another after 10 drachms: in both of these cases the animals were of a smallish size. In two good-sized animals the injection of an ounce did not thus lead to immediate death, and did not produce any alteration in the state of the urine as far as regards sugar. Having carried the experiments further, however, I find that when the injection is pushed to the fullest extent that the animal will safely bear, a saccharine state of the urine is the result. I will give the particulars of two experiments in which

this occurred. I may mention, in passing, that where I have had occasion to give chloroform after the injection of an acid into the circulation, I have found the animal most easily killed by a very small dose, and artificial respiration not of its usual avail in restoring animation.

A good-sized healthy dog which had not been fed the day of the experiment: the urine withdrawn gave no indication of the presence of sugar: $1\frac{1}{2}$ ounce of the Pharmacopœia phosphoric acid diluted with an equal quantity of water injected slowly into one of the jugular veins. The injection was made so slowly that it occupied half an hour in being effected. In one hour's time from the completion of the injection, the urine was highly charged with sugar, giving a copious orange-red reduction with the copper solution.

A large and strong terrier-dog, not fed since twenty-four hours previous to the experiment: 2 ounces and 2 drachms of phosphoric acid diluted with an equal quantity of water, introduced slowly into one of the jugular veins. This was as much as the animal would bear without seriously endangering its life. The urine, twenty minutes after the completion of the injection, was slightly charged with sugar, and one hour and three quarters afterwards pretty highly so.

It is thus evident that when a sufficient quantity of acid is introduced into the circulatory system, the operations of life are so altered that sugar appears in the blood to such an extent as to occasion a strongly marked saccharine state of the urine. From all that I have seen, it appears to me reasonable to conclude that this result is due to a perverted condition of the processes belonging to the liver. The unnatural state of the blood occasioned by the presence of the acid seems to induce the change of amyloid substance into sugar. It seems to promote that change, the result of chemical action, which occurs with such activity after death, and which must be held in abeyance under natural circumstances during life, sugar being found in the system to so scarcely an appreciable extent.

When the quantity of acid used has been large, the blood nearly loses its power of coagulating. In some of my experiments, also, I have noticed that such a morbid state has been induced as to lead to an escape of blood from the vessels during life. I have met with ecchymosis of the liver and stomach, an accumulation of blood in the stomach and intestine, and the presence of blood in the urine.

Looking upon the effect of the acid injection as due to an action upon the liver, it occurred to me that this organ might be much more directly influenced by injecting the acid into a branch of the portal system instead of the jugular vein. It happens, however, that a circumstance occurs to render this mode of experimenting unsuccessful. Although I have never found the acid lead to a solidification of the blood in the vessels when introduced into the general circulation (indeed, as I have mentioned, the effect is the reverse of this), yet when injected into the portal system it causes the blood belonging to this system to solidify and the vessels to become so plugged up that the circulation of portal blood is completely stopped. I have made five experiments in this way; and in all but one the effect referred to has occurred. In three of the cases the acid was used undiluted, but injected very slowly into one of the mesenteric veins; and, in each, under an ounce was used: in the fourth, 6 drachms of the acid diluted with 12 drachms of water formed the injection employed. All the dogs died in less than one hour and a half, and the trunk of the portal vein with its larger divisions in the liver was found plugged up with solidified blood, so as entirely to check the circulation. The tissue of the liver was in places white and hard, as if it had been chemically acted upon by the acid. There was no sugar to be detected in the urine; and the liver, submitted to an ordinary examination after death, behaved in the usual way. From one experiment I learnt that the effect produced by the acid in solidifying the portal blood instantly occurred on the first portion of the injection being made; so that the portal circulation was at once stopped, which would account for the absence of any sugar in the urine.

In the experiment where the circulation remained free, $\frac{1}{2}$ an ounce of the acid was used diluted with 2 ounces of water. The injection was slowly made. The urine in an hour and a half's time was found to contain a slight amount of sugar. Two hours after the injection, when life was destroyed, the liver was perfectly natural in appearance, and all the vessels were free. There was therefore no engorgement of the spleen nor blackening of the intestine from congestion, as was the case in the other experiments.

Finding this mode of experimenting proved unavailable, I next tried the effect of introducing the acid into the alimentary canal instead of directly into the portal system. Injecting it into the stomach

was of no use, for it very soon induced vomiting and was rejected. Half an ounce of the phosphoric acid injected through a tube passed down the œsophagus I found rapidly to occasion repeated vomiting efforts, the stomach having been previously empty. Resorting to the use of chloroform, I therefore introduced the acid into the duodenum, or some other portion of the small intestine.

I have the record before me of the five experiments of this kind that I have performed. They in the most striking manner show that an excess of acid in the system occasions the production of saccharine urine. The following are the leading points belonging to these experiments.

No. 1. In a medium-sized dog, which had not been fed for twenty-four hours, 2 ounces of phosphoric acid were injected into the upper part of the small intestine in $\frac{1}{2}$-ounce portions at intervals of half an hour. Half an hour after the last half ounce had been injected, the life of the animal was destroyed. The bladder was found distended with urine, which gave a strong reaction of sugar. It had been ascertained that it was previously free from this principle. The liver presented an ordinary appearance and behavour. There was no plugging up of the portal vessels; indeed the blood, which was collected during the *post-mortem* examination, scarcely possessed any coagulating property.

No. 2. Fourteen drachms of phosphoric acid were introduced into the duodenum of a largish dog which had not been fed since the day previous. In an hour and a half's time there was a large quantity of urine in the bladder, and it presented a strong reaction of sugar.

No. 3. A medium-sized dog three hours after food: 10 drachms of phosphoric acid injected into the duodenum; urine in two hours' time gave an orange-yellow reduction with the copper solution. Ten drachms more were now again injected, and two hours afterwards the life of the animal was destroyed. The urine gave a still stronger reaction of sugar, namely, an orange-red reduction with the copper solution. The liver presented a natural appearance. The blood collected from the heart had undergone no coagulation whatever by the following day.

No. 4. A small dog five hours after food: 4 drachms of phosphoric acid injected into the duodenum. In one hour and a half the animal was killed. The urine did not contain any sugar. The liver looked

natural, and behaved in the ordinary manner. The blood underwent its usual coagulation.

No. 5. A medium-sized dog that had not been fed for twenty-four hours: 30 drachms of phosphoric acid injected into the duodenum, and two hours afterwards the life of the animal was destroyed. There was no urine found in the bladder. The intestine looked black, as if in a state of mortification. Some of the large venous trunks in the liver were plugged up with coagulated blood. The liver, examined a short time after death, gave only a moderately strong reaction of sugar, and none of the presence of amyloid substance.

It will be observed that in the first three experiments saccharine urine was produced by the influence of phosphoric acid introduced into the intestine. In the fourth, no sugar was found; because, I apprehend, the quantity of acid employed (4 drachms) was too small. The fifth is incomplete, on account of there having been no urine to test; but this experiment is of interest, in showing that a large quantity of the acid injected into the intestinal canal may produce the same kind of effect, as regards plugging up the larger veins of the liver, as when introduced directly into a branch of the portal system.

From a consideration of all that has been brought forward, it is evident that the presence of an acid in sufficient amount in the system so perverts the normal processes of life as to occasion a considerable production of sugar, which, passing into the blood, escapes by the urine. Such is the fact; and, as I have already stated, I consider it to be caused by an effect of the acid upon the liver. The chemical disposition of the amyloid substance to transform into sugar is, I conceive, allowed to come into play from the unnatural state of the blood, and thus the result occurs.

In former communications to the Royal Society, I have mentioned that destruction of the superior cervical ganglia of the sympathetic occasions a temporary diabetes, and that this diabetes is prevented by the previous introduction of carbonate of soda into the circulation. In accordance with what might be expected, the injection of the acid and the operation on the sympathetic produce conjointly a saccharine state of the urine, as either does separately. In one case where I analysed the urine, I found 7·3 grains of sugar per ounce, an hour and a half after the operation on the nerve and the injection had been effected.

I consider it a point of interest (which, however, I merely mention

at present without any comment upon it), that I have observed a jaundiced condition produced by the operation on the sympathetic with the injection of the acid. The urine has been deeply tinged with bile, and has given the characteristic play of colours upon the addition of nitric acid. In the experiments with the injection of the acid alone, it has been a matter of constant observation that a flow of bile has been excited into the duodenum and towards the stomach, the pyloric extremity of which has been highly tinged of a yellow colour.

Although a diabetic state of the urine may be thus artificially induced, apparently by the direct chemical agency of an acid upon the liver, yet I am not prepared to say that, beyond the addition of another significant fact to our knowledge upon this matter, any at present available assistance has been gained towards unravelling the nature of the diabetic disease. Possibly in some cases an insufficiently alkaline state of the portal blood may be the cause of a temporary slightly saccharine state of the urine; but from the observations I have conducted upon diabetics, I certainly am not permitted to think that such is the cause of the well-marked diabetic disease. The immediate cause of the production of sugar in idiopathic diabetes, and in diabetes artificially produced by operations upon the nervous system (the sympathetic and cerebro-spinal), still remains an open point for discovery.

Usually in my experiments with the acid injections the liver has been found fairly charged with amyloid substance; but in a few instances an absence of this principle has been observed, although only a short time has elapsed between the injection and the period of destruction of life.

X. "On the Chemical and Physical Conditions of the Culture of Cotton." By J. W. Mallet, Ph.D., F.C.S., Professor of Chemistry in the Medical College of Alabama. Communicated by Robert Mallet, Esq., F.R.S. Received June 4, 1861.

(Abstract.)

This communication embraces the first portion of an elaborate physical and chemical investigation, in which the author has been and is still engaged, upon the scientific conditions involved in the successful agriculture of the cotton plant. To this train of research he has